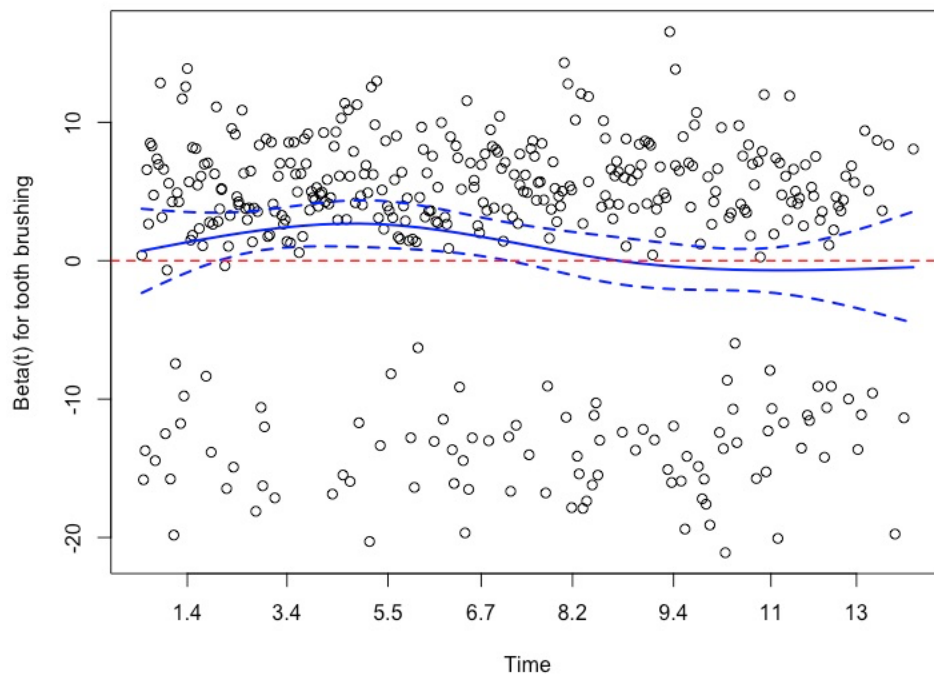


Supplementary Material – Oral health and risk of upper gastrointestinal cancers in a large prospective study from a high-risk region: Golestan Cohort Study

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Supplementary Figure

Figure S1. Plot of the scaled Schoenfeld residuals against the Kaplan-Meier transformed time for the association between tooth brushing and gastric cancer. The blue solid line shows the natural spline fit, along with confidence bands at two standard errors shown by the blue dotted lines. The red dotted line at $y = 0$ has been added for reference.



Supplementary Tables

Table S1. Meta-analysis results of the association between oral health variables and the upper gastrointestinal cancers combined. All models were adjusted for age, sex, socioeconomic score, ethnicity, residence, education, cigarette use, and opium use. The model for tooth loss was also adjusted for denture use.

		HR	95% CI	p-value
Brushing	Never	Reference		
	Non-daily	0.809	(0.643, 1.02)	0.0698
	Daily	0.706	(0.565, 0.882)	0.00218
Tooth loss	Expected or less	Reference		
	Q1	0.969	(0.781, 1.20)	0.773
	Q2	1.02	(0.808, 1.28)	0.892
	Q3	1.26	(1.01, 1.58)	0.0447
	Q4	1.61	(1.20, 2.15)	0.00132
DMFT	Expected or less	Reference		
	Q1	0.879	(0.728, 1.06)	0.177
	Q2	0.974	(0.782, 1.21)	0.811
	Q3	1.25	(0.983, 1.60)	0.0682
	Q4	1.12	(0.849, 1.48)	0.422

Table S2. Associations between frequency of tooth brushing and gastric cancer at different time intervals of follow-up: ≤ 4 years (early), > 4 and ≤ 7 years (mid), > 7 years (late). Adjusted for age, sex, socioeconomic score, ethnicity, residence, education, cigarette use, and opium use.

Time interval	Brushing	HR	95% CI	p-value
Early	Never	Reference		
	Non-daily	0.607	(0.304, 1.21)	0.156
	Daily	0.458	(0.229, 0.918)	0.0277
Mid	Never	Reference		
	Non-daily	0.714	(0.368, 1.39)	0.320
	Daily	0.541	(0.278, 1.05)	0.0708
Late	Never	Reference		
	Non-daily	0.914	(0.588, 1.42)	0.689
	Daily	1.01	(0.689, 1.49)	0.943

Table S3. Associations between frequency of tooth brushing and cancers of the esophagus and stomach, and the two sites combined [i.e., upper gastrointestinal (UGI) cancers], from sensitivity analyses excluding the first two years of follow-up. All models were adjusted for age, sex, socioeconomic score, ethnicity, residence, education, cigarette use, and opium use. Associations with esophageal cancer were also adjusted for tea temperature.

	Brushing	HR	95% CI	p-value
Esophagus	Never	Reference		
	Non-daily	0.909	(0.649, 1.27)	0.581
	Daily	0.697	(0.493, 0.986)	0.0415
	Linear trend	0.845	(0.717, 0.996)	0.0448
	Global trend			0.124
Stomach	Never	Reference		
	Non-daily	0.767	(0.541, 1.09)	0.138
	Daily	0.749	(0.540, 1.04)	0.0828
	Linear trend	0.852	(0.727, 0.999)	0.0487
	Global trend			0.113
UGI	Never	Reference		
	Non-daily	0.833	(0.653, 1.06)	0.139
	Daily	0.714	(0.563, 0.906)	0.00553
	Linear trend	0.844	(0.753, 0.946)	0.00349
	Global trend			0.0138

Table S4. Associations between tooth loss and cancers of the esophagus and stomach, and the two sites combined [i.e., upper gastrointestinal (UGI) series], from sensitivity analyses excluding the first two years of follow-up. All models were adjusted for age, sex, socioeconomic score, ethnicity, residence, education, cigarette use, opium use, and denture use. Associations with esophageal cancer were also adjusted for tea temperature.

	Tooth loss	HR	95% CI	p-value
Esophagus	Expected or less	Reference		
	Q1	1.02	(0.729, 1.42)	0.923
	Q2	0.926	(0.645, 1.33)	0.679
	Q3	1.21	(0.850, 1.71)	0.292
	Q4	1.47	(0.943, 2.30)	0.0892
	Linear trend	1.07	(0.975, 1.18)	0.152
	Global trend			0.376
Stomach	Expected or less	Reference		
	Q1	0.888	(0.638, 1.24)	0.482
	Q2	1.13	(0.804, 1.58)	0.489
	Q3	1.24	(0.884, 1.74)	0.213
	Q4	1.59	(1.03, 2.44)	0.0348
	Linear trend	1.10	(1.00, 1.20)	0.0440
	Global trend			0.173
UGI	Expected or less	Reference		
	Q1	0.953	(0.754, 1.20)	0.687
	Q2	1.03	(0.807, 1.32)	0.799
	Q3	1.23	(0.966, 1.57)	0.0924
	Q4	1.54	(1.13, 2.09)	0.00647
	Linear trend	1.09	(1.02, 1.16)	0.0128
	Global trend			0.0497

Table S5. Associations between DMFT and cancers of the esophagus and stomach, and the two sites combined [i.e., upper gastrointestinal (UGI) series], from sensitivity analyses excluding the first two years of follow-up. All models were adjusted for age, sex, socioeconomic score, ethnicity, residence, education, cigarette use, and opium use. Associations with esophageal cancer were also adjusted for tea temperature.

	DMFT	HR	95% CI	p-value
Esophagus	Expected or less	Reference		
	Q1	0.918	(0.684, 1.23)	0.569
	Q2	0.995	(0.704, 1.41)	0.975
	Q3	1.52	(1.07, 2.16)	0.0196
	Q4	1.02	(0.651, 1.59)	0.938
	Linear trend	1.05	(0.963, 1.15)	0.262
	Global trend			0.129
Stomach	Expected or less	Reference		
	Q1	0.882	(0.665, 1.17)	0.382
	Q2	0.946	(0.681, 1.31)	0.738
	Q3	1.11	(0.769, 1.61)	0.570
	Q4	1.12	(0.757, 1.66)	0.565
	Linear trend	1.02	(0.942, 1.11)	0.591
	Global trend			0.785
UGI	Expected or less	Reference		
	Q1	0.899	(0.733, 1.10)	0.305
	Q2	0.969	(0.764, 1.23)	0.797
	Q3	1.30	(1.01, 1.68)	0.0408
	Q4	1.08	(0.802, 1.45)	0.619
	Linear trend	1.04	(0.976, 1.10)	0.241
	Global trend			0.150

Table S6. Associations between oral health variables and esophageal squamous cell carcinoma. Adjusted for age, sex, socioeconomic score, ethnicity, residence, education, cigarette use, opium use, and tea temperature. The model for tooth loss was also adjusted for denture use.

		HR	95% CI	p-value
Brushing	Never	Reference		
	Non-daily	0.933	(0.661, 1.32)	0.696
	Daily	0.787	(0.560, 1.11)	0.168
	Linear trend	0.893	(0.759, 1.05)	0.173
	Global trend			0.384
Tooth loss	Expected or less	Reference		
	Q1	1.02	(0.730, 1.42)	0.922
	Q2	0.924	(0.643, 1.33)	0.668
	Q3	1.16	(0.806, 1.66)	0.430
	Q4	1.44	(0.907, 2.30)	0.122
	Linear trend	1.06	(0.962, 1.17)	0.241
	Global trend			0.498
DMFT	Expected or less	Reference		
	Q1	0.799	(0.594, 1.07)	0.138
	Q2	0.938	(0.665, 1.32)	0.718
	Q3	1.38	(0.960, 1.98)	0.0822
	Q4	0.832	(0.511, 1.35)	0.459
	Linear trend	1.01	(0.921, 1.11)	0.844
	Global trend			0.0943

Table S7. Associations between frequency of tooth brushing and gastric cardia and noncardia cancers. Adjusted for age, sex, socioeconomic score, ethnicity, residence, education, cigarette use, and opium use.

	Brushing	HR	95% CI	p-value
Cardia	Never	Reference		
	Non-daily	0.702	(0.444, 1.11)	0.129
	Daily	0.621	(0.399, 0.968)	0.0353
	Linear trend	0.775	(0.625, 0.960)	0.0194
	Global trend			0.0558
Noncardia	Never	Reference		
	Non-daily	0.881	(0.547, 1.42)	0.600
	Daily	0.897	(0.583, 1.38)	0.623
	Linear trend	0.940	(0.761, 1.16)	0.565
	Global trend			0.809

Table S8. Associations between tooth loss and gastric cardia and noncardia cancers. Adjusted for age, sex, socioeconomic score, ethnicity, residence, education, cigarette use, opium use, and denture use.

	Tooth loss	HR	95% CI	p-value
Cardia	Expected or less	Reference		
	Q1	0.670	(0.427, 1.05)	0.0812
	Q2	0.921	(0.590, 1.44)	0.716
	Q3	1.21	(0.786, 1.86)	0.388
	Q4	1.28	(0.705, 2.32)	0.418
	Linear trend	1.05	(0.931, 1.18)	0.439
	Global trend			0.251
Noncardia	Expected or less	Reference		
	Q1	1.23	(0.796, 1.90)	0.350
	Q2	1.30	(0.810, 2.08)	0.279
	Q3	1.32	(0.814, 2.13)	0.262
	Q4	1.98	(1.12, 3.52)	0.0190
	Linear trend	1.15	(1.01, 1.30)	0.0324
	Global trend			0.217

Table S9. Associations between DMFT and gastric cardia and noncardia cancers. Adjusted for age, sex, socioeconomic score, ethnicity, residence, education, cigarette use, and opium use.

	DMFT	HR	95% CI	p-value
Cardia	Expected or less	Reference		
	Q1	0.556	(0.381, 0.811)	0.00232
	Q2	0.805	(0.534, 1.21)	0.301
	Q3	0.687	(0.398, 1.19)	0.179
	Q4	1.25	(0.770, 2.02)	0.371
	Linear trend	0.976	(0.875, 1.09)	0.663
	Global trend			0.0177
Noncardia	Expected or less	Reference		
	Q1	1.41	(0.951, 2.09)	0.0871
	Q2	1.18	(0.738, 1.90)	0.483
	Q3	1.63	(0.994, 2.68)	0.0527
	Q4	1.31	(0.749, 2.29)	0.344
	Linear trend	1.10	(0.980, 1.23)	0.105
	Global trend			0.259